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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/656,915	09/07/2000	Larry I. Benowitz	CMZ-129	2385

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EXAMINER	
GAMETT, DANIEL C	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 09/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/656,915	BENOWITZ, LARRY I.	
	Examiner	Art Unit	
	Daniel C. Gamett, PhD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32,33,36,37 and 58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32,33,36,37 and 58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Examiner for your application in the USPTO is now Daniel C. Gamett, Ph.D., Art Unit 1647.

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/25/2005 has been entered. Claims 1-31, 34, 35, and 38-57, are cancelled. Claims 32, 33, 36, 37, and 58 are under examination.

Withdrawn Objections And/Or Rejections

2. Objections to Claims 33 and 34 as being dependent upon a rejected base claim and Claims 36 and 37 as being dependent upon a cancelled claim, set forth in the Final Rejection mailed 11/23/2004 are withdrawn in view of Applicant's amendments.

3. Rejection of claim 32 under 35 U.S.C. 112, second paragraph, regarding the limitation "human", is withdrawn in view of Applicant's amendments.

4. Rejections of Claims 31, 32, and 58 under 35 U.S.C. 102(a) as being anticipated by Zhou *et al.*, claim 58 under 35 U.S.C. 102(b) as being anticipated by Adler *et al.*, and claim 58 under 35 U.S.C. 102(b) as being anticipated by Rowland-Gagne & Greene, are withdrawn in view of Applicant's amendments.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhou *et al.*, J Biol Chem. 275(4): 2513-9 (of record in IDS #B11).

a. Claim 33 is drawn to an in vitro method comprising contacting N-kinase with a test compound and determining the ability of the test compound to increase or decrease N-kinase dependent phosphorylation of a substrate, wherein the N-kinase is bovine N-kinase.

b. Zhou *et al.* teach the cloning and characterization of human MST3b kinase, which is equivalent to N-kinase (see instant Specification pp. 6 lines 19-27). Zhou *et al.* performed *in vitro* kinase assays using MBP as substrate and tested the ability of at least one compound (PKA) in alter MST3b activity (paragraph spanning pp. 2517 and 2518, for example), thus meeting the limitations of claim 33 except that the N-kinase of Zhou *et al.* was not bovine N-kinase. However, Zhou *et al.* demonstrated that their human nucleic acid probes could detect brain-specific expression of homologous sequences in rat brain (fig. 2). The use of bovine brain as a source for the biochemical purification of enzymes of the nervous system is a common practice in the art (see, for example, Cheung and Minglin, Methods in Enzymology, Volume 38 , 1974, Pages 223-239). Bovine brains are

readily available through slaughterhouses and provide abundant starting material for such purifications. Therefore, it would have been obvious to one of skill in the art at the time the invention was made to use bovine brain as a readily available, abundant source of mammalian N-kinase and to perform assays as taught by Zhou *et al.* to study the regulation of N-kinase activity.

7. Claim 58, 32, 36, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Volante *et al.*, J. Cell Biology, 109:2395-2403, November 1989 (of record in IDS, #B9) in view of Zhou *et al.*, J Biol. Chem. 275(4): 2513-9 (of record in IDS, #B11) and Benowitz *et al.* J Biol. Chem. 273(45):29626-29634, November 6, 1998.

a. Claim 58 is drawn to an *in vitro* method of identifying a compound that stimulates or inhibits axonal growth of a central nervous system neuron by increasing or decreasing human N-kinase dependent phosphorylation of a substrate by selecting a test compound that increases or decreases human N-kinase dependent phosphorylation of a substrate and contacting a CNS neuron, *in vitro*, with said selected test compound.

b. Volante *et al.* tested several compounds for effects on N-kinase activity (table 1, figure 5) and for effects on neurite outgrowth (figures 6 and 7, table II) for the purpose of investigating a possible correlation between the two effects. The differences between Volante *et al.* and instant claim 58 are that (1) PC12 cells are not central nervous system neurons and (2) PC12 cells are a rat cell line and therefore the N-kinase being studied was not human.

c. Benowitz *et al.* teach that 6-thioguanine (6-TG), known from Volante *et al.* to inhibit N-kinase in PC12 cells, inhibits axon outgrowth in rat retinal ganglion cells and that

inosine overcomes the inhibitory effect of 6-TG (fig. 7). Therefore, Benowitz *et al.* chose compounds for study based on their known effects on N-kinase and examined the selected compounds for effects on axon outgrowth, which reads on instant claim 58 with the exception that the N-kinase in question was not human.

d. Zhou *et al.* established that human and rat homologs of N-kinase are structurally equivalent in that nucleic acid probes derived from human sequences specifically recognize rat mRNA (figure 2) and that rat N-kinase is expressed in CNS neurons (p. 2515, right column, first two full paragraphs).

e. Therefore, the combined teachings of Volante *et al.* and Benowitz *et al.* suggest a correlation between N-kinase and axon outgrowth; both Benowitz *et al.* and Zhou *et al.* teach CNS neurons; and Zhou *et al.* teach human N-kinase. Together these references indicate that the method of claim 58 would have been obvious to one of ordinary skill in the art at the time the invention was made. One of ordinary skill in the art would have been motivated to combine these teachings to employ CNS neurons (as opposed to PC12 pheochromocytoma cells) and a human enzyme in order to achieve a system that models human physiology more precisely than could be achieved by the existing models.

f. Claim 32 is drawn to a variation of the method of claim 58 in which the N-kinase is recombinantly produced. Zhou *et al.* teach recombinantly expressed MST3b (fig. 3 and associated text beginning on p. 2515), the human equivalent of N-kinase. It would have been obvious to one of ordinary skill in the art at the time the invention was made to recombinantly produce human N-kinase, as suggested by Zhou *et al.*, with the motivation of having a readily available, pure preparation for use in the testing method.

g. Absent evidence to the contrary, one of ordinary skill in the art at the time the invention was made would have expected some test compounds to increase (claim 37) and others to decrease (claim 36; see for example 6-TG in Volante *et al.* Tables 1 and II) N-kinase activity.

Conclusion

8. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C Gamett, Ph.D., whose telephone number is 571 272 1853. The examiner can normally be reached on M-F, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571 272 0961. The fax phone number for the organization where this application or proceeding is assigned is 571 273 8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DCG
Art Unit 1647
8 September 2005

Brenda Brumback
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